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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/817,328	DING ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 15-19* is/are pending in the application.

4a) Of the above claim(s) *2-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-12 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission, which included cancellation of claims 2-5, 13, 14 and amendment to claims 1, 6-11 and 18, filed on 5/2/2007 has been entered. Claims 1, 6-12 and 15-19 are now under consideration. Claims 2-5 were withdrawn as noted in the previous office action. In view of applicants' response, 112 second paragraph rejection, 112 first paragraph written description rejection and prior art 102 & 103 rejections made in the previous office action have been obviated. However, 112 first paragraph rejections and double patenting rejections are maintained and new ground of rejections applied to currently pending claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-12 and 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of "any aryl" in R^3 definition of claim 1 and 7-10 renders claims 1, 7-10 and its dependent claims 6, 11, 12 and 15-19 indefinite, as there is no aryl in the definition of R^3. It is unclear what is intended.

2. Claim 8 is an improper dependent claim as it fails to further limit claim 1 on which it is ultimately dependent. Note the choice of naphthyl recited in claim 8 is not included in claim 1.

3. Currently amended claim 18 is an improper claim as it now relates to non-elected subject matter. Note only isomeric pyrimidines (X^1 or X^2 is nitrogen, the other CR^4) were elected not triazine in paper dated 11/9/2005.

4. Recitation of "compounds" in claims 6-10 render these claims indefinite, as it is not clear whether these claims are compound claim or a composition claims containing the compounds of claim 1. Replacement of "compounds" with "compound" is suggested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 6-12 and 15-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making pharmaceutically acceptable salts does not reasonably provide enablement for making solvate or hydrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. **The nature of the invention and the state of the prior art:**

The invention is drawn to compound of formula I, or a pharmaceutically acceptable salt solvate or hydrate thereof. Specification is not adequately enabled as to how to make hydrate of compounds of formula (I) Specification has no example of hydrate of the instant compounds. Specification on page 6 and 15 recites solvate or hydrate thereof but there is no enabling of such compounds.

The compound of formula I embrace pyrimidine compounds substituted with variable groups R^1, R^2, R^3 and R^4.

Even a cursory calculation of the number of compounds embraced in the instant formula (I) based on the generic definition of alkyl., aryl heteroaryl, heterocyclyl, substituted aryl, heteroaryl, arylalkyloxy, arylalkylthio etc would result in hundreds of thousands of compounds. This is of course not the accurate number and the true number of compounds would far exceed this number of compounds. Thus the genus embraced in the claim 1 is too large and there is no teaching of any hydrate or solvate of this large genus.

Search in the pertinent art, including water as solvent resulted in a pertinent reference, which is indicative of unpredictability of hydrate formation in general. The state of the art is that is not predictable whether solvates or hydrates will form or what their composition will be. In the language of the physical chemist, a hydrate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. Compared with polymorphs, there is an additional degree of freedom to hydrates, which means a different solvent or even the moisture of the air that might change the stabile region of the hydrate. In the instant case of hydrate a similar reasoning therefore apply. Water is a solvent and hence it is held that a pertinent detail of West, which relates to solvates, is also applicable to hydrate

In addition, an additional search resulted in Vippagunta et al., Advanced Drug Delivery Reviews 48: 3-26, 2001, which clearly states that formation of hydrates in unpredictable. See entire document especially page 18, right column section 3.4. Note Vippagunta et al., states "Each solid compound responds uniquely to the possible

formation of solvates or hydrates and hence generalizations cannot be made for series of related compounds".

2. **The predictability or lack thereof in the art:**

Hence, the solvate and hydrate as applied to the above-mentioned compounds claimed by the applicant are not art-recognized compounds and hence there should be adequate enabling disclosure in the specification with working example(s).

3. **The amount of direction or guidance present:**

Examples illustrated in the experimental section are limited to making the compounds not related to solvates and hydrates. There is no example of a solvate or hydrate of instant compound. One hundred and twenty-six compounds were shown in the examples of the specification each of which has come in contact with water and other solvent but there is no showing that instant compounds formed solvates or hydrates. Hence it is clear that merely bring the compound with solvent or water does not result in solvate or hydrate and additional direction or guidance is needed to make them Specication has no such direction or guidance.

4. **The presence or absence of working examples:**

There is no working example of any solvate or hydrate formed. The claims are drawn to hydrate, yet the numerous examples presented all failed to produce a solvate or hydrate or even hydrate. These cannot be simply willed into existence. As was stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there, is no evidence that such

compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ...' no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that hydrates of these compounds actually exists; if they did, they would have formed. Hence, there should be showing supporting that solvates and hydrates of these compounds exist and therefore can be made.

5. **The breadth of the claims & the quantity of experimentation needed:**

Specication has no support, as noted above, for compounds generically embraced in the claim 1 would lead to desired solvate and hydrate of the compound of formula I. As noted above, the genus embraces over million compounds and hence the breadth of the claim is broad. The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired hydrate of compound of formula I embraced in the instant claims in view of the pertinent reference teachings.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is

clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

This rejection is same as made in the previous office action but limited to currently pending claims. Applicants' traversal to overcome this rejection is not persuasive for reasons of record. As for the traversal, the following apply.

First of all, as stated above, specification has no showing the large genus of compounds of claim 1 formed hydrate or solvate. Over 126 compounds are disclosed, each of which have been in contact with water and solvent yet no solvate or hydrate formed. Thus bring a compound to water or solvent during recrystallisation or otherwise did not lead solvate or hydrate. Hence, specification has no enablement for solvate or hydrate.

Secondly, contrary to applicants' assertion, there is no evidence in the non-patent literature that solvate or hydrate would form with any compound. The formation of hydrate or solvate is unpredictable as noted in references cited by the examiner. Applicants have argued that interaction with water often results in hydrate but instant compounds have been in interaction with water and there is no evidence in the specification that they formed hydrate. As for Vippugunta, the article clearly states hydrate or solvate formation is no predictable. Applicants have inserted the word "predictably" but it is not there on page 15. In fact the next paragraph clearly states "mere presence of water in the system is not sufficient reason to expect hydrate formation...". As for Stahl et al. , a careful analysis would show that issue is not predictability but a finding that on third of compounds examined formed hydrate. Thus,

two-third did not form hydrate and therefore there is no predictability of formation of hydrate or solvate. Again, the issue is does instant compound form hydrate or solvate not which pharmaceutical formed hydrate or solvate.

Hence, based on these considerations, the rejection is deemed as proper and is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11 and 15-16 are rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating leukemia, does not reasonably provide enablement for treating any or all tumoral disease generically embraced in these claims as well as well as inhibiting Bcr-abl with any compound and thereby treating any all diseases or disorders generically embraced in the claim language. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims.

The instant method of use claims 15-16 and the pharmaceutical claim 11 with the intended use are drawn to inhibiting Bcr-abl and thereby treating any or all diseases. Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of bcr-abl by the instant compounds, claims 11 and 15-16 are reach through treating any or all tumoral diseases in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of bcr-abl, it is claimed that treating any or all tumoral diseases in general. The scope of the claims includes any or all tumoral diseases due to Bcr-abl inhibition including those yet to be discovered as due said mode of action for which there is no enabling disclosure. In addition, the scope of treatment of tumoral diseases would include treatment of various cancers including group consisting of lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region. stomach cancer, colon cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system (CNS), primary CNS lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, or a combination of one or more of the foregoing cancers, which is not

adequately enabled solely based on the activity of the compounds provided in the specification. The instant compounds are disclosed to have receptor tyrosine kinase inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all diseases stated above for which applicants provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action as tyrosine kinase inhibitor that would be useful for all sorts of tumoral diseases. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as psoriasis, lung cancer, brain cancer, pancreatic cancer, colon cancer etc. are very difficult to treat and despite the fact that there are many anticancer drugs.

The scope of the claims involves millions of compounds of claim 1 as well as the thousand of diseases embraced by the terms tumoral diseases.

Tumoral disease would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by the Helicobacter pylori infection of ulcers.

Cancer is just an umbrella term. Tumors vary from those so benign that they are never treated to those so virulent that all present therapy is useless.

No compound has ever been found to treat tumoral diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is

contrary to our present understanding of oncology. Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally.

Also see the PTO website

<<http ://www.uspto.gov/web/offices/pac/dapp/1 pecba.htm#7>>

ENABLEMENT DECISION TREE, Example F, situation 1) which is directed to the scope of cancers.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Mass, R. D., Int. J. Radiation Oncology Bio. Phys.Vol. 58(3): 932-940, 2004 and Fabbro et al. Pharmacology & therapeutics 93, 79-98, 2002.

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating tumoral diseases that require receptor tyrosine kinase inhibitory activity.

2) The state of the prior art: Recent publications expressed that the receptor tyrosine kinase inhibition effects are unpredictable and are still exploratory. See Mass et al. and Fabbro et al., cited above especially the concluding paragraph.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all tumors by the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the

degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all tumoral diseases and the state of the art is that the effects of tyrosine kinase inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace treatment of any or all tumoral diseases with large genus of compounds.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make

and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

This rejection is same as made in the previous office action and is maintained for reasons of record. As for applicants' traversal, the following is applied:

Claims 11, 15, and 16 are reach through claims. Based on the mode of action of the instant compounds as inhibitor of Bcr-abl, the claims reach through in treating any disease for which there is no enabling disclosure.

Specification has no support for treating any or tumors as recited in claim 11 or treating any or diseases generically embraced in the claim language. Prior are also does not support this contention. This is an incredible finding for which applicants have not provided supporting evidence.

In addition, claim 15, which also recites inhibiting Bcr-abl by any or all compounds that bind to myristoyl binding pocket, is clearly a reach through claim, for which there is no enabling disclosure. Specification has no teaching or suggestion that which compound would bind to said binding pocket and the pool of "compound" being very very large as it includes any compound, one has to do extensively undue experimentation to arrive at which compound would inhibit Bcr-abl and among them which would do so by binding to the said pocket. The showing that some of the instant compounds inhibit Bcr-abl activity by binding to the said pocket cannot be extrapolated to any compound much less to the instant huge genus of compounds.

Hence, this rejection is proper and is therefore maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6-8,11 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Ikeda et al., US 4,849,424.

Ikeda et al. teaches several pyrimidine compounds of formula I for treating peptic ulcer which include instant compounds. See column 1, formula 1 and note the definition of X, Y, R^1, R^2 and R^3 groups. Especially note when X or Y is nitrogen, the other carbon and R^3 is aryloxy, the compound taught by Ikeda include instant compound when instant L= bond and R^1=OR^7. Also note aryloxy include, phenoxy, tolyoxy, xyloxy and naphthoxy and also not various heteroaryl choices of R^1 and R^2. See column 2, line 32 for a species. See entire document for details of the invention and process of making. See example 21.

Claims1, 6-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Aldrich et al., US 6,342,503.

Aldrich et al. teaches several pyrimidine compounds useful for treating anxiety, which include instant compounds. See column 6, formula 1 and note the definition of various variable groups V, Y, Z, J, K, L, M, X, R^1, R^3 and R^4. Especially note with the given definition of V, Y, Z, JKLM ring and R^1 and R^3 clearly overlaps with the definition

of instant R^1, L-R^3, R^2 and R^4 groups and compounds taught by Aldrich et. al. therefore include instant compounds. See column 2-17 for further details of the invention, 18-23 for various species, 34-73 for process of making shown in Schemes 1-28, column 73-111 for examples 1-105. Especially see column 113-122, Table 1 and column 131-132 , Table 11 for species of compounds, which include instant compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6-8,11 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ikeda et al., US 4,849,424.

Teachings of Ikeda et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Ikeda et al. teaches several pyrimidine compounds of formula I for treating peptic ulcer which include instant compounds. See column 1, formula 1 and note the definition of X, Y, R^1, R^2 and R^3 groups. Especially note when X or Y is nitrogen, the other carbon and R^3 is aryloxy, the compound taught by Ikeda include instant compound when instant L= bond and R^1=OR^7. Also note aryloxy include, phenoxy, tolyoxy, xyloxy and naphthoxy and also not various heteroaryl choices of R^1 and R^2. See column 2, line 32 for a species. See entire document for details of the invention and process of making. See example 21.

Ikeda et al. differs in exemplifying not all compounds generically embraced in the compound of formula I. However, Ikeda et al. teaches equivalency of those compounds taught in column 5-9, examples 1-21 with those generically recited in column 1 for compound of formula I. See definition of X, Y, R^1, R^2 and R^3 groups.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Ikeda et al and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1, 6-11 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over- Aldrich et al., US 6,342,503.

Teachings of Aldrich et al. as discussed in the above 102 rejection is incorporated herein.. As noted above, Aldrich et al. teaches several pyrimidine compounds useful for treating anxiety, which include instant compounds. See column 6, formula 1 and note the definition of various variable groups V, Y, Z, J, K, L, M, X, R^1, R^3 and R^4. Especially note with the given definition of V, Y, Z, JKLM ring and R^1 and R^3 clearly overlaps with the definition of instant R^1, L-R^3, R^2 and R^4 groups and compounds taught by Aldrich et. al. therefore include instant compounds. See column 2-17 for further details of the invention, 18-23 for various species, 34-73 for process of making shown in Schemes 1-28, column 73-111 for examples 1-105. Especially see column 113-122, Table 1 and column 131-132, Table 11 for species of compounds, which include instant compounds.

Aldrich et al. differs in exemplifying not all compounds generically embraced in the compound of formula I. However, Aldrich et al. teaches equivalency of those compounds taught in column 73-132 with those generically recited in column 1 for compound of formula I. See definition of V, Y, Z, J, K, L, M, X, R^1, R^3 and R^4 groups.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Aldrich et al and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Election/Restrictions

This application contains claims 2-5 were drawn to an invention nonelected with traverse in the reply filed on 11/19/2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6-12 and 15-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 57-72 of copending Application No. 10/270,030. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter namely aryl substituted pyrimidines embraced in the instant claims are also embraced in the copending application 10/270,030.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection is same as made in the previous office action. Applicants have differed addressing the rejection till the application is indicated as in condition for allowance. The rejection is proper and is maintained.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

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7/10/2007